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Comparing the efficacy and safety of Sri Lankan traditional medicine regimen for knee osteoarthritis

Submission date
24/07/2021

Recruitment status
No longer recruiting

Registration date
03/08/2021

Overall study status
Completed

Last Edited
28/11/2023

Condition category
Musculoskeletal Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Osteoarthritis (OA) has become a burden globally for the healthcare sector due to the number of people developing or living with the condition. Knee osteoarthritis (KOA) is the most common form of arthritis causing disability and impaired quality of life especially in the elderly. The WHO report on priority diseases and reasons for inclusion 2018, provides an in-depth review of the various diseases or conditions including osteoarthritis in its chapter sixth has been selected and grouped according to the nature of the pharmaceutical gap(s) associated with it. The Osteoarthritis Research Society International (OARSI) also identified OA as a serious disease and one of their major concerns is treatments for osteoarthritis. There are numerous drug treatments for osteoarthritis; however, their efficacy and adverse effect profiles often limit their use. Currently, pharmacological (drug), non-pharmacological, and surgical measures are considered in the treatment of OA with the aim of reducing pain and improving the function of the knee joint. At present, there is no proven disease-modifying therapy or cure available for OA.

Sri Lankan Traditional Medicine regimens are widely used to treat OA and there are many treatment regimens including decoctions, pills, pastes, and fermentation procedures recorded which may be effective for the long-term management of OA. The aim of this study is to compare the clinical efficacy and safety of Sri Lankan Traditional Medicine to conventional treatment for KOA

Who can participate?
Adults aged 40 years or older with a diagnosis of knee osteoarthritis.

What does the study involve?
Participants will be allocated to one of two groups, with an equal chance of being in either group (like tossing a coin). One group will receive Sri Lankan Traditional Medicine treatment for KOA and the other will receive conventional treatment for KOA. Participants will receive treatment for up to 8 weeks and will be asked to complete an Osteoarthritis diary card of their symptoms and attend the clinic twice weekly. Participants will also be assessed at 1 and 2 months after finishing treatment.

What are the possible benefits and risks of participating?
The participants receive information and advice from a specialized medical team. In addition, their participation may help to develop an Ayurveda drug treatment for osteoarthritis.

All adverse events experienced by patients will be recorded regularly after two weeks by the investigators at every visit to the clinic. Further, patients will be advised to record any adverse reactions in their patient diaries and will be advised to inform the investigators using the given contact numbers. They will also be advised to come to the clinic for assessment when they have any unexpected symptoms or complaints. If any serious adverse events occur, they will be carefully assessed and reported to the ERC of IIM within 5 working days. No serious adverse reactions are expected with any of the two study medications. However, in the events of an adverse reaction requiring in-hospital management, the facilities and expert management would be provided and the complete clinical trial will be terminated prematurely if there is evidence that the safety of the trial participants can no longer be assured or new scientific information arises during the course of the clinical trial regarding patient safety.

All patients' records will be kept safely and securely (in a cupboard the access which is limited to the principal investigator and co investigators). Identification data of patients will be encrypted by using a participant code. The study will be conducted adhering to Good Clinical Practice (GCP) guidelines. Protocol modifications will be informed to Ethics Review Committees for their approval and informed to the trial registry.

Where is the study run from?
Institute of Indigenous Medicine, University of Colombo (Sri Lanka)

When is the study starting and how long is it expected to run for?
From August 2019 to August 2024

Who is funding the study?
Institute of Indigenous Medicine, University of Colombo (Sri Lanka)

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Two arm open-label noninferiority randomized control clinical trial for comparing the efficacy and safety of Sri Lankan traditional medicine regimen for knee osteoarthritis

Study objectives
Sri Lankan Traditional Medicine therapies improve pain and have disease-modifying effects in patients with knee osteoarthritis (KOA)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 22/12/2020, Ethics Review Committee, Institute of Indigenous Medicine (ERCIIM) (Institute of Indigenous Medicine, University of Colombo, Rajagiriya, Sri Lanka; +94 (0)112692395 ext.407; ethicsreviewiim@gmail.com), ref: ERC/20/105 (https://iim.cmb.ac.lk/erciim/)

Study design
Two arm open-label noninferiority randomized controlled clinical trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Knee osteoarthritis

Interventions
This will be a two-arm open-label non-inferiority randomized control trial in patients with knee osteoarthritis. A consecutive consenting sample method will be followed to select participants of the arms for the study. A blocked design will be used, using an online statistical computing web programming to generate the randomization schedule (research randomizer https://www.randomizer.org). Eligible subjects will be randomly assigned to either Arm I or Arm II

The patients of the Arm I will be treated with herbal decoction (Rasnadvigunabhagasya or Maharasnadi decoction) 120 ml twice a day before meals for 50 days, herbal pill (Yogaraja Guggulu) 1000 gms twice a day before meals for 50 days, herbal paste (Sandivadam Lepaya) sufficient amount for knee daily for 30 days and herbal fomentation (Kumburuetaperumkayam Pottani) daily for 30 days. The patients of Arm II will receive hot water fomentation after applying 1% Diclofenac sodium gel daily for 30 days and Tablet Paracetamol 500 mg twice daily after meals for 60 days and Tablet Ibuprofen 200 mg twice daily after meals for 60 days. Patients in both arms will be asked to visit the clinic twice weekly.

The Western Ontario and McMaster Universities Arthritis Index (WOMAC) and the Knee Injury and Osteoarthritis Outcome Score (KOOS) of the patients will be the primary efficacy endpoint after 12 weeks. The 10 point improvement will be compared between the two arms as the primary endpoint at the end of 2 months of the treatment at the follow-up visits. WOMAC subscales, a pain disability index, a visual analog scale for pain and sleep quality, a quality-of-life index will be used as secondary endpoints in the clinical trial. These symptom scores will be analyzed by using the information mentioned in the Osteoarthritis diary card of the patient. These diary cards will be collected twice a week at the clinic. Patients will be assessed at follow-up visits at the clinic after 1 and 2 months without drug intervention.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Herbal decoction of Rasnadvigunabhagasya, herbal paste and herbal fomentation and 1% diclofenac gel, Tablet paracetamol, and Ibuprofen

Primary outcome(s)
Current primary outcome measure as of 04/08/2022:

The primary endpoint is a percentage change in the score on the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) measured at the baseline and the end of the intervention (after 8 weeks).

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Previous primary outcome measure:

Knee symptoms and function measured using the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) and the Knee Injury and Osteoarthritis Outcome Score (KOOS) at baseline, 12 weeks, and 4 and 5 months

Key secondary outcome(s))
Current secondary outcome measures as of 04/08/2022:

Change in Knee Injury and Osteoarthritis Outcome Score (KOOS), a pain disability index, a visual analog scale for pain and sleep quality, a
quality-of-life index (The World Health Organization (WHO) , The WHOQOF : https://www.who.int/tools/whoqol) measured at the baseline and the end of the intervention (after 8 weeks and 1 month, 2month and 3 month of follow-up).

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Previous secondary outcome measures:

1. Knee pain, function, and stiffness measured using WOMAC subscales at baseline, 12 weeks, and 4 and 5 months

2. Impact of knee pain measured using the pain disability index at baseline, 12 weeks, and 4 and 5 months
3. Pain measured using a visual analog scale (VAS) at baseline, 12 weeks, and 4 and 5 months
4. Sleep quality measured using a visual analog scale (VAS) at baseline, 12 weeks, and 4 and 5 months
5. Quality of life measured using the quality-of-life index at baseline, 12 weeks, and 4 and 5 months

Completion date
11/08/2024

Eligibility

Key inclusion criteria
Diagnosis and classification of knee osteoarthritis (KOA) based on history, clinical examination findings, and classical radiological findings as follows:
1. The three American College of Rheumatology (ACR) classification criteria for the knee shown below, but for this study the lower age limit will be reduced from 50 years to 40 years:
1.1. ACR Clinical classification criteria, where KOA is classified by the presence of knee pain along with at least three of the following six items:
1.1.1. Aged >50 years
1.1.2. Morning stiffness <30 min
1.1.3. Crepitus on knee motion
1.1.4. Bony tenderness
1.1.5. Bony enlargement
1.1.6. No palpable warmth
1.2. ACR Clinical/Radiographic classification criteria, where KOA is classified by the presence of knee pain with at least one of the following three items along with osteophyte in knee X-Ray:
1.2.1. Aged >50 years
1.2.2. Morning stiffness <30 min
1.2.3. Crepitus on knee motion
1.3. ACR Clinical/Laboratory classification criteria, where KOA is classified by the presence of knee pain along with at least 5 of the following 9 items:
1.3.1. Aged >50 years
1.3.2. Morning stiffness <30 min
1.3.3. Crepitus on knee motion
1.3.4. Bony tenderness
1.3.5. Bony enlargement
1.3.6. No palpable warmth
1.3.7. Rheumatoid Factor <1:40
1.3.8. Erythrocyte sedimentation rate (ESR) <40 mm/h
1.3.9. Synovial fluid compatible with OA
2. Visual Analogue Score (VAS) for pain mean pain intensity in one or both knees of ≥40 mm on a 100 mm while performing a weight-bearing activity (walking, standing, or climbing a staircase) over the 7 days before baseline assessment. The VAS used will be a five-point Likert scale version with five response levels for each item, representing different degrees of intensity: None (0), mild (1), moderate (2), severe (3), and extreme (4).
3. Radiographic evidence of OA grades 1-3 assessed using the ranking score of the Kellgren-Lawrence radiographic system (0-4)

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
50 years

Sex
All

Key exclusion criteria
1. Non-degenerative joint diseases or other joint diseases such as rheumatoid arthritis, psoriatic arthritis, gonococcal arthritis, and haemoarthritis
2. Severe disabling arthritis and/or are bedridden
3. History of intra-articular knee injection within the month preceding the study
4. Evidence of severe unstable cancer, hypertension, cardiac disorder, mental health disorder, or renal, hepatic, diabetic, or haemopoietic disease revealed by history and/or investigation
5. Concurrent anticoagulant/antiplatelet drugs, corticosteroids, or narcotic pain killers use
6. History of epilepsy or bleeding disorders, gastric ulcers, renal or hepatic disease, uncontrolled hypertension, or body mass index (BMI) >45 kg/m²
7. A washout period of 7 days is required for NSAID users
8. Discontinuing the use of common complementary and alternative therapies for arthritis (e.g. glucosamine, chondroitin sulfate, bromelain, DMSO, acupuncture, and Ayurveda medicine) is required for 7 days prior to enrollment
9. Written informed consent to participate in the study not provided

Date of first enrolment
10/08/2021

Date of final enrolment
11/05/2024

Locations

Countries of recruitment
Sri Lanka

Study participating centre
National Ayurveda Teaching Hospital
Borella, Colombo 08
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Sponsor information

Organisation
University of Colombo

ROR
https://ror.org/02phn5242

Funder(s)

Funder type
University/education

Funder Name
Institute of Indigenous Medicine, University of Colombo

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr RHSK de Silva (dr.himalee@iim.cmb.ac.lk). Study participant data sheets will not include contact or identifying details. Study data entry and study management systems used by clinical sites will be secured and password protected. At the end of the study, all study databases will be de-identified and archived. Availability of raw data of the study is based on above conditions.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		22/11/2022	28/11/2022	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes